July 16, 2014

The Honorable Joseph R. Pitts
Chairman
Subcommittee on Health
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Pitts:

Thank you again for the opportunity to testify before the Subcommittee on Health on the "21st Century Cures: Examining the Role of Incentive in Advancing Treatments and Cures for Patients." As a follow up to your request, below are my responses to the questions asked by several members of the committee.

The Honorable Joseph R. Pitts

1. **The size and cost of clinical trials is an impediment to investment and innovation, particularly for products treating diseases that impact large patient populations. How can advances in technology make trials more efficient?**

   In-line with the significant advancements made in computer science and information technology, computational modeling and simulation have positively impacted device development and reduced the time to verify and validate the performance of breakthrough technologies. Such methods also have potential to revolutionize the field with regards to clinical trials, but have not been leveraged to their full potential due to historical perspectives and regulatory requirements related to animal and human studies. Leveraging technological advances and modeling will not only allow new ideas to be tested with greater confidence and decreased cost, but will also allow medical device clinical trials to be conducted while reducing risk to patients.

2. **Understanding that lengthy clinical trials with a large number of participants are currently the norm for drugs treating chronic diseases such as heart disease and stroke, what processes does FDA have in place to provide the necessary certainty to sponsors up front so that, when resources are devoted to drug development in these areas, investors and companies can plan accordingly?**

   As a reminder, my area of focus/expertise is more medical device focused than drug focused. With that said, I believe the question holds true for medical device clinical trials addressing chronic diseases as well. If a sponsor successfully meets the endpoints of an FDA approved clinical trial (via the IDE process), it is essential that the FDA remain true to its word and approve the product. Moving goal posts will prevent manufacturers from pursuing such studies if there remains uncertainty on approval even if the agreed upon endpoints are met. Progress has been made in this area and the FDASIA bill is expected to help. With that said, it remains essential that these obligations are met.

   Additionally, I would reference back to your first question. Solutions to improve clinical trial efficiency are likely to be most impactful in the areas of chronic disease. Post-marketing studies can also play a role in this area as well.

3. **To date, CMS has declined to provide guidance regarding the extent to which changes may be made to a durable medical equipment (DME) product such that it remains a "modified" or "upgraded" product subject to the grandfathering provision of the three-year minimum lifetime requirement (MLR) for DME, and not a "new" product that may no longer be eligible for reimbursement as DME. What is the impact of this lack of guidance on Medicare beneficiary access to innovative medical devices?**

   The fact that medical device manufacturers cannot make any reasonable inferences regarding whether modifications or upgrades to their existing DME products will push these products outside the DME benefit is a significant threat to Medicare beneficiary access to the best medical technologies. Medical device development is an iterative process whereby products are continually assessed for potential improvements for the benefit of patient health and experience – and for opportunities to reduce healthcare costs. The current lack of guidance on the application of the grandfathering provision of the three-year MLR for DME seriously stifles innovation of medical devices, which detrimentally affects Medicare beneficiary access to the most advanced medical technologies. More specifically, It is believed that the limited guidance CMS has chosen to provide has discouraged manufacturers from investing in medical innovation. Even with the agency's proposed clarification to the grandfathering provision of the three-year MLR, it is believed that manufacturers will not be allowed to introduce technological advancements to their products without the threat of losing Medicare coverage.

4. **What are your recommendations for DME reimbursement policy regarding the application of the grandfathering provision of the three-year MLR that continues to promote and foster innovation of medical devices?**

   CMS should consider avoiding a "one-size fits all" policy regarding the grandfathering provision that fails to recognize the wide and complex array of DME products covered by the three-year MLR. The proposed grandfathering policy should be applied in a way that would allow continued Medicare coverage of "modified" products as DME even though they may continue to have an expected life of less than three years (as was historically the case before the products were modified). It is suggested that CMS convene a study panel to examine at a minimum the following central questions:

   - Must a "modified" item fall within the same HCPCS code and/or DME product category as a grandfathered item in order for it to also fall within the grandfathering provision?

   - Would a premarket approval (PMA) product approved after January 1, 2012 that is similar in structure and function to grandfathered products be considered a "modified" version of the grandfathered products? Is a newly-cleared 510(k) product considered to be a "modified" version of a predicate device?

   - What modifications can be made to a grandfathered product (including products with disposable components) that would result in more efficient and effective treatments (and thereby improve the health of Medicare beneficiaries) but reduce the minimum lifetime of the product?

   In short, it is recommended that CMS, in its continued implementation of the three-year MLR, instead promote policies that create incentives for manufacturers to make innovative modifications

to medical devices that will improve the health of Medicare beneficiaries and thereby lower costs to the Medicare program.

The Honorable Michael C. Burgess

1. **Would you comment on some of the barriers that Class III medical device manufacturers face when seeking coverage and payment from CMS for innovative cutting edge technology that improves the lives of patients?**

While the unpredictability of the FDA has been of primary concern in recent years, we are now most concerned with the risk presented by ensuring a new technology will be covered and paid for, both by public and private insurers. Securing coverage and payment for Class III medical devices is a very complex and unpredictable process and can add an additional three to five years more before patients can benefit from a new product. This issue is, in part, due to the difference in statutory missions of FDA and CMS – being that FDA requires demonstrated safety and effectiveness, while CMS needs assurance that the new technology is reasonable and necessary for beneficiaries, resulting in the need for additional and expensive human trials. However, in recent years, increased difficulty in achieving coverage by public and private insurers for new medical devices and diagnostics has been observed.

Historically, medical device manufacturers have been able to leverage FDA sponsored clinical trials for submission to payers (CMS and private payors) to gain reimbursement for innovative products. This, however, no longer appears to be the case. There is increasing evidence that payors are raising the standard for coverage determinations. One study by Tufts University researchers found that the probability a therapy considered for national coverage under the Medicare program will be approved dropped by more than 60 percent between 1999 and 2007. When coverage was granted, the scope was more limited than the indications approved by the FDA in 40 percent of the cases studied.[1] While Medicare national coverage determinations represent a relatively limited universe, we are finding that both private payors and government programs are increasing the bar for coverage and reimbursement decisions. What is most troubling is that it is often not clear where that bar lies.

The overall process of obtaining coverage and reimbursement represents a classic "chicken and the egg" dilemma for the investment community. On the one hand, payors want to see more data and diffusion of a new technology until they agree to provide coverage for it. On the other, physicians and hospitals will not agree to use the product unless they get paid. Equally challenging, the data and utilization requirements these organizations require for approval are ambiguous at best. They are unwilling to commit in advance to reimburse a product downstream if clearly defined endpoints are met. It becomes a never-ending process fraught with risk and uncertainty.

Given these challenges, we need to make the coverage process in both the public and private payor context more open and transparent. We need to take steps to expedite coverage and reimbursement decisions. We need to foster improved collaboration among the innovator, payor and patient communities. And we need to ensure that our government programs are more receptive to rapid coding and coverage of new technologies. Specific recommendations can be found in my testimony.

The solution is not to move back from appropriate incentives to provide high value care or to suggest that products that do not offer therapeutic benefits should be covered; rather it is to make the public policy changes necessary to assure that the new emphasis on cost does not result in the unintended and unwanted consequence of undermining development and adoption of new and better treatments.

The Honorable Cathy McMorris Rodgers

1. **Would you explain the evaluation that a VC does of a medical device start-up? Are looking at how promising the idea is, what the outlook is for FDA approval, whether or not CMS will cover the device, or a combination of factors? How has this continuum changed over the last 10-15 years?**

   Venture capitalists make investment decisions in medical device start-ups based upon our level of confidence that we can generate a meaningful return on the investment for our investors (i.e., Limited Partners). To generate a meaningful return, the dollars out (from an exit) must be more than the dollars in (from our investment). This also must occur within a reasonable period of time (4-6 years) and with a reasonable probability of success (30% - 40% of our companies historically fail/do not return capital).

   As such, venture capitalists evaluate the factors that affect the nature of the exit (i.e., timing, size, and M&A or IPO), the level of investment, and the probability of success. Factors affecting the nature of the exit include the level of unmet clinical need, the strength of the team, market size, strategic relevance, strength of intellectual property, level of competition, and likely inflection point when an IPO or acquisition will occur. Factors affecting the level of investment include technical complexity, clinical complexity, regulatory path, reimbursement path, commercialization path and again the strength of the team. Lastly, factors affecting risk often touch on each of the elements noted above (i.e., what is the likelihood our assumptions will prove true). As venture capitalists, we are willing to take risk on one or two key items but we tend to shy away from opportunities that have multiple or compounded risks.

   Over the past 10-15 years, the dollars required to build a medical device company have grown considerably (now >$100 million) while the dollars received at the time of exit have remained steady or actually fallen. Similarly, timelines have lengthened (now 8-10 years) and the probability of success has fallen (now 50% - 60% of our companies will fail/not return capital). All of these factors result in an investment profile where the "math" no longer works and the sector is no longer an attractive investment opportunity for our investors.

   The reasons for this decline are varied, but at its core, it can be attributed to four main factors: 1) increased timelines and data requirements by FDA, 2) increased timelines and data requirements by CMS and private payers, 3) increased regulatory requirements, and 4) an unfavorable tax environment. As discussed in my testimony, progress has been made with FDA (although our work is by no means complete). We now need to make progress in the other areas as well.

The Honorable Gus Bilirakis

1. **Your testimony mentioned that FDA allows for the use of novel endpoints, biomarkers and non-traditional clinical trial designs, but lacks transparency and consistency in their approach. How**

can we improve the process and encourage regulators to use every tool in their proverbial toolbox?

I believe this point actually relates more to drug clinical development and is likely to be better addressed by Alexis Borisy (who also testified). My area of focus/expertise tends to be more medical device focused.

2. **One mechanism drug companies have to improve certainty about the agency's acceptance of certain trial designs is to enter into a Special Protocol Assessment (SPA) agreement, which was first authorized in 2007 for that very purpose. Have these agreements generally brought the intended certainty to companies and has the agency always held up its end of the binding contract?**

   Once again, this point relates to drug clinical development and is likely better addressed by Alexis Borisy from Third Rock Ventures.

3. **What barriers are currently in place that limit the potential of using clinical and outcomes data to learn about how therapies are working on patients in the real world? How should we address them?**

   I don't have an answer to this question at this time.

4. **In your testimony, you touch on the need for certainty after approval and the challenge of ensuring that there is coverage of a new drug or device by Medicare, Medicaid or private insurance. Typically, commercial insurers cover something that Medicare covers. Would you talk about some of the challenges that are faced getting covered and reimbursed under Medicare?**

   See Question 1 from the Honorable Michael C. Burgess.

Thank you again for your leadership on this important initiative and please let me know if I can provide you with any additional information.

Sincerely,

Mike Carusi
General Partner
Advanced Technology Partners

[1] Chambers J.D., Morris S, Neumann P, and Buxton M. (March 2012) Factors Predicting Medicare National Coverage: An Empirical Analysis. *Medical Care Journal*, 50(3).